PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference REP07631WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/05049	International filing date *(day/month/year)* 20.11.2003	Priority date *(day/month/year)* 20.11.2002
International Patent Classification (IPC) or both national classification and IPC A61K38/00		
Applicant ARRIVA-PROMETIC INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18.06.2004	04.02.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Engl, B Telephone No. +49 89 2399-8283

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/05049

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-41	as originally filed

Claims, Numbers

1-33	as originally filed
34-36	received on 22.12.2004 with letter of 21.12.2004

Drawings, Sheets

1/2-2/2	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	34
	No:	Claims	1-33,35,36
Inventive step (IS)	Yes:	Claims	34
	No:	Claims	1-33,35,36
Industrial applicability (IA)	Yes:	Claims	see separate sheet
	No:	Claims	

2. Citations and explanations

   see separate sheet

Concerning Section V:

1. The following prior art is cited from the International Search Report:

D1: DATABASE WPI Section Ch, Week 198242 Derwent Publications Ltd., London, GB; Class A96, AN 1982-88806E & JP 57 145817
D2: GB-A-2 318 732
D3: WO 99/49887
D4: WO 00/07620
D5: EP-A-0 420 600
D6: WO 99/02665
D7: WO 01/30380
D8: WO 01/64132
D9: WO 92/06706

D1 describes a pharmaceutical composition for treating peptic ulcer comprising aprotinin, hydroxypropyl cellulose and sodium CMC, and optionally gelatin.

D2 describes hydrogel or slow release maxtrix formulations comprising alpha-1-antitrypsin (i.e. alpha-1-proteinase inhibitor) along with cellulose derivatives, polyacrylic acids (page 2 lines 5-9), alginate, collagen, or a synthetic bioabsorbable polymer (page 2 lines 13 and 22), and their use for treating chronic wounds or ulcers (page 1, lines 26-27).

D3 describes compositions for treating wounds comprising protease inhibitors, preferably in the form of a cellulose gel (page 3, lines 22-30).

D4 describes compositions for treating psoriasis comprising a PAI-2 inhibitor, preferably together with another serine protease inhibitor in a cellulose gel formulation (page 4, lines 17-27), optionally in phosphate-buffered saline solution (page 7, line 18).

D5 discloses compositions for use as an ophthalmologic, otolaryngologic or dermatologic medicament which comprises at least one protease inhibitor, a buffer (column 2, line 48), thickeners, such as (hydroxypropyl) methyl cellulose, polyvinylpyrrolidone, polyvinyl alcohol, poly(meth)acrylamides etc (column 3, lines 10-14), and may further comprise antiphlogistics or antibiotics (column 3, lines 26-43).

D6 describes HIV protease inhibitors with a cellulosic surface stabilizer which may be formulated as a gel (page 5, line 21) and may comprise buffers, celluloses, polyvinylpyrrolidone, acacia, alginic acid, carrageenin and other hydrocolloids (page 7, lines 8-17).

D7 describes ophthalmologic formulations comprising a protease inhibitor which can be alpha-1-antitrypsin (page 20, line 30), can be formulated as a gel (page 27, line 23), be buffered (page 27, line 21) and lyophilized (page 27, line 27), and can contain biodegradable, biocompatible polymers (page 27, line 34 - page 28, line 15).

D8 describes compositions for healing wounds which comprise protease inhibitors, such as alpha-antitrypsin (page 8, line 8) and come in the form of films, hydrocolloids, hydrogels, composite of fibres containing polysaccharides, polyurethane copolymers, polyvinylpyrrolidone etc (page 9, line 25 - page 10, line 10).

D9 describes the administration of serine protease inhibitors, such as antitrypsin and antichymotrypsin, for treating mast cell implicated diseases. Example I discloses a topical cream for the treatment of (inter alia) psoriasis, example III discloses a solution comprising 1000 mg of a composition comprising 70% alpha-1-antitrypsin and 10-18% alpha-1-antichymotrypsin in 50 ml saline solution for treating atopic dermatitis.

2. The cited prior art is considered to anticipate the present claimed subject-matter; those embodiments which are possibly novel would not be considered inventive since compositions comprising protease inhibitors and gelling agents are already known from the prior art. In particular, D9 is considered to anticipate claims 35 and 36.

Novelty and inventive step (Article 33 (2) and (3) EPC) cannot therefore be acknowledged for claims 1-33 and 35, 36.

Claim 34 is considered both novel and inventive since the use of alpha-1-antitrypsin for treating ichthyosis has been neither taught nor suggested by the available prior art.

Claims 16-33 might be objected to because they are directed to methods of therapeutic treatment.